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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:25:29 ON 26 AUG 2008

=> fil .bio

FILE 'MEDLINE' ENTERED AT 07:25:43 ON 26 AUG 2008

FILE 'BIOSIS' ENTERED AT 07:25:43 ON 26 AUG 2008
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FILE 'CAPLUS' ENTERED AT 07:25:43 ON 26 AUG 2008
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FILE 'EMBASE' ENTERED AT 07:25:43 ON 26 AUG 2008
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=> e axen a/au
E1            2     AXEMO PIA DR/AU
E2            1     AXEMOON T/AU
E3            2 --> AXEN A/AU
E4            1     AXEN ALFRED/AU
E5           45     AXEN ANDREAS/AU
E6            1     AXEN ANETTE/AU
E7            6     AXEN ANNKRISTIN H/AU
E8            1     AXEN B/AU
E9           12     AXEN C/AU
E10           2     AXEN CHRISTINA/AU
E11           1     AXEN CLAES/AU
E12         500     AXEN D/AU

=> s e3
L1            2 "AXEN A"/AU

=> s e5
L2           45 "AXEN ANDREAS"/AU

=> e baumann h/au
E1            3     BAUMANN GWENDALYN C/AU
E2            1     BAUMANN GWENDALYN CHAMPION/AU
E3         1275 --> BAUMANN H/AU
E4            5     BAUMANN H A/AU
E5            2     BAUMANN H D/AU
E6            7     BAUMANN H DR/AU
E7           17     BAUMANN H E/AU
E8            1     BAUMANN H E DR/AU
E9            1     BAUMANN H G/AU
E10           1     BAUMANN H H JR/AU
E11          16     BAUMANN H J/AU
E12           3     BAUMANN H M/AU

=> s e3-e12
L3         1328 ("BAUMANN H"/AU OR "BAUMANN H A"/AU OR "BAUMANN H D"/AU OR "BAUMANN
H DR"/AU OR "BAUMANN H E"/AU OR "BAUMANN H E DR"/AU OR "BAUMANN H G"/AU OR "BAUMANN
H H JR"/AU OR "BAUMANN H J"/AU OR "BAUMANN H M"/AU)
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=> e e12
E1            1     BAUMANN H H JR/AU
E2           16     BAUMANN H J/AU
E3            3 --> BAUMANN H M/AU
E4            9     BAUMANN H N JR/AU
E5           13     BAUMANN H P/AU
E6            1     BAUMANN H PROF/AU
E7           73     BAUMANN H R/AU
E8            5     BAUMANN H W/AU
E9            1     BAUMANN HALWACHS GABRIELE/AU
E10           1     BAUMANN HANNA/AU
E11           1     BAUMANN HANNE MERETE/AU
E12           1     BAUMANN HANNELORE/AU

=> s e4-e8
L4          101 ("BAUMANN H N JR"/AU OR "BAUMANN H P"/AU OR "BAUMANN H PROF"/AU OR
"BAUMANN H R"/AU OR "BAUMANN H W"/AU)

=> e baumann herb/au
E1            1     BAUMANN HENRY P/AU
E2            1     BAUMANN HENRY R JR/AU
E3            0 --> BAUMANN HERB/AU
E4           72     BAUMANN HERBERT/AU
E5            1     BAUMANN HERBERT HUBERT/AU
E6            3     BAUMANN HERLIND/AU
E7            7     BAUMANN HERMAN P/AU
E8            2     BAUMANN HERMANN/AU
E9            1     BAUMANN HERVE/AU
E10           1     BAUMANN HINNERK/AU
E11           1     BAUMANN HINRICH/AU
E12           1     BAUMANN HOELZLE RUTH/AU

=> s e4-e5
L5           73 ("BAUMANN HERBERT"/AU OR "BAUMANN HERBERT HUBERT"/AU)

=> e carredano e/au
E1            1     CARRECNO NEFTALI L V/AU
E2            1     CARRECO P/AU
E3            4 --> CARREDANO E/AU
E4           34     CARREDANO ENRIQUE/AU
E5            2     CARREDDU P/AU
E6            1     CARREDO V/AU
E7            9     CARREE FABIEN/AU
E8            2     CARREE GILLES/AU
E9            1     CARREE HENRI/AU
E10           1     CARREE I A/AU
E11           1     CARREE J Y/AU
E12           1     CARREE JEAN YVES/AU

=> s e3-e4
L6           38 ("CARREDANO E"/AU OR "CARREDANO ENRIQUE"/AU)

=> s l1-l6
L7         1559 (L1 OR L2 OR L3 OR L4 OR L5 OR L6)

=> s l7 AND ((igg OR immunoglobulin OR antibod OR fab OR k-fab OR kappa-
fab)(5a)(constant))
L8            1 L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR KAPPA-
FAB)(5A)(CONSTANT))
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=> s l7 AND ((igg OR immunoglobulin OR antibod OR fab OR k-fab OR kappa-
fab)(15a)(constant))
L9          2 L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR KAPPA-
FAB)(15A)(CONSTANT))

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10           2 DUP REM L9 (0 DUPLICATES REMOVED)

=> d ibib ed abs l10 1-2

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2004:392488  CAPLUS  Full-text
DOCUMENT NUMBER:          140:405484
TITLE:                    Immunoglobulin G constant region binding pocket for
screening and/or designing chemical entities capable of selective binding to IgG
INVENTOR(S):              Axen, Andreas; Baumann, Herbert; Carredano, Enrique
PATENT ASSIGNEE(S):       Amersham Biosciences Ab, Swed.
SOURCE:                   PCT Int. Appl., 63 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     --------------      ----   --------    -------------------     --------
     WO 2004039843        A1    20040513    WO 2003-SE1435          20030912
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO,
CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
     AU 2003259008        A1    20040525    AU 2003-259008          20030912
PRIORITY APPLN. INFO.:                     SE 2002-3226        A   20021031
                                           WO 2003-SE1435      W   20030912

ED   Entered STN:  14 May 2004
AB   The present invention relates to a human IgG binding pocket comprised of a
     first interacting surface, which originates from an IgG k light chain, and a
     second interacting surface, which originates from an IgG heavy chain, which
     amino acids are strictly conserved between human IgGs of κ-type.  The
     invention also embraces an isolated and purified polypeptide, which comprises
     said binding pocket.  Further, the invention relates to various methods of
     using the novel binding pocket, such as in screening for identification of
     chemical entities capable of selective binding thereof, and in other exptl.
     and/or virtual methods for design and/or identification of chemical entities
     capable of selective binding thereof.
REFERENCE COUNT:          3      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2004:390212  CAPLUS  Full-text
DOCUMENT NUMBER:          140:390281
TITLE:                    Urea variants as affinity ligands for IgG
INVENTOR(S):              Axen, Andreas; Baumann, Herbert; Carredano, Enrique;
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Groenberg, Anna; Steensma, Elles
PATENT ASSIGNEE(S): Amersham Biosciences Ab, Swed.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039765	A1	20040513	WO 2003-SE1434	20030912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003259007	A1	20040525	AU 2003-259007	20030912
US 20060014735	A1	20060119	US 2005-531783	20050418

PRIORITY APPLN. INFO.:

SE 2002-3226	A	20021031
SE 2002-3878	A	20021220
WO 2003-SE1434	W	20030912

OTHER SOURCE(S): MARPAT 140:390281
ED Entered STN: 13 May 2004
AB The present invention relates to an IgG-binding compound, which more specifically has affinity for human IgGs of k-type and functional derivs. thereof. More specifically, the compound according to the invention comprises an N,N-alkylated urea moiety located between an aromatic part and another part, which is a linear or cyclic substituted or unsubstituted aliphatic group. The compound binds to a pocket-shaped binding site present on all human IgGκ Fabs, which site is located between the two domains (CH1 and CL) of its constant part. Accordingly, the compound according to the invention is a ligand for human IgGs of κ-type, and consequently, the invention also relates to a separation matrix for affinity chromatog., which matrix comprises said compound, as well as to other uses of the compound
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l7 AND ((igg OR immunoglobulin OR antibod OR fab OR k-fab OR kappa-fab)(10a)(ch1))
L12 5 L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR KAPPA-FAB)(10A)(CH1))

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 2 DUP REM L12 (3 DUPLICATES REMOVED)

=> d ibib ed abs l13 1-2

L13 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:390212 CAPLUS Full-text
DOCUMENT NUMBER: 140:390281
TITLE: Urea variants as affinity ligands for IgG

INVENTOR(S): Axen, Andreas; Baumann, Herbert; Carredano, Enrique; Groenberg, Anna; Steensma, Elles
PATENT ASSIGNEE(S): Amersham Biosciences Ab, Swed.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039765	A1	20040513	WO 2003-SE1434	20030912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003259007	A1	20040525	AU 2003-259007	20030912
US 20060014735	A1	20060119	US 2005-531783	20050418
PRIORITY APPLN. INFO.:			SE 2002-3226	A 20021031
			SE 2002-3878	A 20021220
			WO 2003-SE1434	W 20030912

OTHER SOURCE(S): MARPAT 140:390281
ED Entered STN: 13 May 2004
AB The present invention relates to an IgG-binding compound, which more specifically has affinity for human IgGs of k-type and functional derivs. thereof. More specifically, the compound according to the invention comprises an N,N-alkylated urea moiety located between an aromatic part and another part, which is a linear or cyclic substituted or unsubstituted aliphatic group. The compound binds to a pocket-shaped binding site present on all human IgGκ Fabs, which site is located between the two domains (CH1 and CL) of its constant part. Accordingly, the compound according to the invention is a ligand for human IgGs of κ-type, and consequently, the invention also relates to a separation matrix for affinity chromatog., which matrix comprises said compound, as well as to other uses of the compound
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004272091 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15152083
TITLE: A novel and conserved pocket of human kappa-Fab fragments: design, synthesis, and verification of directed affinity ligands.
AUTHOR: Carredano Enrique; Baumann Herbert; Gronberg Anna; Norrman Nils; Glad Gunnar; Zou Jinyu; Ersoy Oguz; Steensma Elles; Axen Andreas
CORPORATE SOURCE: Amersham Biosciences R&D, Bjorkgatan 30, S-751 84 Uppsala, Sweden.
SOURCE: Protein science : a publication of the Protein Society, (2004 Jun) Vol. 13, No. 6, pp. 1476-88.
Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501

ENTRY DATE: Entered STN: 3 Jun 2004
Last Updated on STN: 12 Jan 2005
Entered Medline: 11 Jan 2005

ED Entered STN: 3 Jun 2004
Last Updated on STN: 12 Jan 2005
Entered Medline: 11 Jan 2005

AB Antibodies of type IgG may be divided into two classes, called lambda or kappa, depending on the type of light chain. We have identified a conserved pocket between the two domains CH1 and CL of human IgG kappa- Fab, which is not present in the lambda type. This pocket was used as a target docking site with the purpose of exploring the possibilities of designing affinity ligands that could function as such even after immobilization to gel. The idea of the design arose mainly from the results of the saturated transfer difference (STD-NMR) screening of 46 compounds identified by means of virtual docking of 60 K diverse compounds from the Available Chemicals Directory (ACD). Surface plasmon resonance (SPR) was used as an alternative method to monitor binding in solution. A total of 24 compounds belonging to a directed library were designed, synthesized, and screened in solution. They consist essentially of an amino acid condensed to a N,N'-methylated phenyl urea. STD-NMR results suggest that a small hydrophobic side chain in the condensed amino acid promotes binding, whereas a hydroxyl-group-containing side chain implies absence of STD-NMR signals. Three compounds of the directed library were immobilized and evaluated as chromatographic probes. In one case, using D-Pro as the condensed amino acid, columns packed with ligand-coupled Sepharose (Amersham Biosciences) retained two different monoclonal samples of kappa-Fab fragments with different variable regions, whereas a sample of monoclonal lambda-Fab fragments was not retained under similar chromatographic conditions.

=> s (ch1-cl OR cl-ch1 OR (ch1(2a)cl))(15a)(constant OR fab)
L15 70 (CH1-CL OR CL-CH1 OR (CH1(2A) CL))(15A)(CONSTANT OR FAB)

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16 36 DUP REM L15 (34 DUPLICATES REMOVED)

=> d ibib ed abs l16 1-36

L16 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:653916 CAPLUS Full-text
DOCUMENT NUMBER: 149:30149
TITLE: Human IgG2 Antibodies Display Disulfide-mediated Structural Isoforms
AUTHOR(S): Wypych, Jette; Li, Ming; Guo, Amy; Zhang, Zhongqi; Martinez, Theresa; Allen, Martin J.; Fodor, Szilan; Kelner, Drew N.; Flynn, Gregory C.; Liu, Yaoqing Diana; Bondarenko, Pavel V.; Speed Ricci, Margaret; Dillon, Thomas M.; Balland, Alain
CORPORATE SOURCE: Department of Analytical Sciences, Amgen Inc., Thousand Oaks, CA, 91320, USA
SOURCE: Journal of Biological Chemistry (2008), 283(23), 16194-16205
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Jun 2008

AB Here, the authors present studies of the covalent structure of human IgG2 mols. Detailed anal. showed that recombinant human IgG2 monoclonal antibody could be partially resolved into structurally distinct forms caused by multiple disulfide bond structures. In addition to the presently accepted structure for the human IgG2 subclass, the authors also found major structures that differ from those documented in the current literature. These novel structural isoforms are defined by the light chain constant domain (CL) and the heavy chain CH1 domain covalently linked via disulfide bonds to the hinge region of the mol. The results demonstrate the presence of 3 main types of structures within the human IgG2 subclass, and the authors have named these structures IgG2-A, -B, and -A/B. IgG2-A is the known classic structure for the IgG2 subclass defined by structurally independent Fab domains and hinge region. IgG2-B is a structure defined by a sym. arrangement of a (CH1-CL-hinge)2 complex with both Fab regions covalently linked to the hinge. IgG2-A/B represents an intermediate form, defined by an asym. arrangement involving one Fab arm covalently linked to the hinge via disulfide bonds. The newly discovered structural isoforms are present in native human IgG2 antibodies isolated from myeloma plasma and from normal serum. Furthermore, the isoforms are present in native human IgG2 with either κ or λ light chains, although the ratios differ between the light chain classes. Thus, disulfide structural heterogeneity is a naturally occurring feature of antibodies belonging to the human IgG2 subclass.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 1

ACCESSION NUMBER: 2008:389030 BIOSIS Full-text

DOCUMENT NUMBER: PREV200800389029

TITLE: Rapid identification of reactive cysteine residues for site-specific labeling of antibody-Fabs.

AUTHOR(S): Junutula, Jagath R. [Reprint Author]; Bhakta, Sunil; Raab, Helga; Ervin, Karen E.; Eigenbrot, Charles; Vandlen, Richard; Scheller, Richard H.; Lowman, Henry B.

CORPORATE SOURCE: Genentech Inc, 1 DNA Way,MS 231B, San Francisco, CA 94080 USA jagath@gene.com; hbl@gene.com

SOURCE: Journal of Immunological Methods, (MAR 20 2008) Vol. 332, No. 1-2, pp. 41-52.
CODEN: JIMMBG. ISSN: 0022-1759.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Jul 2008
Last Updated on STN: 16 Jul 2008

ED Entered STN: 16 Jul 2008
Last Updated on STN: 16 Jul 2008

AB Cysteines with reactive thiol groups are attractive tools for site-specific labeling of proteins. Engineering a reactive cysteine residue into proteins with multiple disulfide bonds is often a challenging task as it may interfere with structural and functional properties of the protein. Here we developed a phage display-based biochemical assay, PHESELECTOR (Phage ELISA for Selection of Reactive Thiols) to rapidly screen reactive thiol groups on antibody fragments without interfering with their antigen binding, using trastuzumab-Fab (hu4D5Fab) as a model system. The solvent accessibility values for all the amino acid residues in the hu4D5Fab were calculated using available crystal structure information. Serine, alanine and valine residues with highest solvent accessibility values were selected and tested to compare structure-based design with the PHESELECTOR biochemical method. Cysteine substitutions at partially solvent-accessible alanine or valine residues exhibited better thiol reactivity values than substitutions at serine residues. The poor correlation between fractional solvent accessibility and

thiol reactivity of the engineered hu4D5Fab variants indicated the value of PHESELECTOR biochemical assay to identify reactive thiol groups on the antibody-Fab surface. Mass spectrometric analysis of biotinylated ThioFab (Fab with engineered cysteine) variants confirmed that conjugation occurred only at the engineered cysteine thiols of either light or heavy chains. ThioFabs with engineered cysteine residues in the constant domains (CL and CH1) should allow universal application for site-specific conjugation of antibody- Fabs. (C) 2007 Elsevier B.V. All rights reserved.

L16 ANSWER 3 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:82637 CAPLUS Full-text
DOCUMENT NUMBER: 146:161483
TITLE: Modified antibody fragments
INVENTOR(S): Humphreys, David Paul
PATENT ASSIGNEE(S): UCB S. A., Belg.
SOURCE: PCT Int. Appl., 28pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007010231	A1	20070125	WO 2006-GB2649	20060717

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2006271416	A1	20070125	AU 2006-271416	20060717
CA 2615485	A1	20070125	CA 2006-2615485	20060717
EP 1913026	A1	20080423	EP 2006-764991	20060717

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS

PRIORITY APPLN. INFO.:	GB 2005-14779	A 20050719
	WO 2006-GB2649	W 20060717

ED Entered STN: 25 Jan 2007
AB The author discloses engineered antibody fragments to which one or more effector mols. may be attached. The engineered antibody fragments are characterized in that the native interchain disulfide bond between the heavy (CH1) and light (CL) chain constant regions is absent and the heavy chain (CH1) and light chain (CL) constant regions are linked by an interchain disulfide bond between a pair of engineered cysteines, one in the light chain constant region and the other in the heavy chain constant region.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 36 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006481321 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16876195
TITLE: Structure-based stability engineering of the mouse IgG1 Fab fragment by modifying constant domains.
AUTHOR: Teerinen Tuija; Valjakka Jarkko; Rouvinen Juha; Takkinen

Kristiina
CORPORATE SOURCE: VTT Biotechnology, P.O. Box 1000, 02044 VTT Espoo, Finland.
SOURCE: Journal of molecular biology, (2006 Aug 25) Vol. 361, No. 4, pp. 687-97. Electronic Publication: 2006-07-28.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 15 Aug 2006
Last Updated on STN: 5 Oct 2006
Entered Medline: 4 Oct 2006
ED Entered STN: 15 Aug 2006
Last Updated on STN: 5 Oct 2006
Entered Medline: 4 Oct 2006

AB A semi-rational approach based on structural data was exploited in a search for CH1 and CL domains with improved intrinsic thermodynamic stabilities. Structural and amino acid level comparisons were carried out against known biophysically well-behaving and thermodynamically beneficial scFv and Fab fragments. A number of mutant Fab fragments were constructed by site-directed mutagenesis of regions in the CH1 and CL domains expected to be most sensitive under physical stress conditions. These mutations were located on three sites in the Fab constant domains; a mobile loop in the CH1 domain, residues surrounding the two largest solvated hydrophobic cavities located in the interface of the CH1 and CL domains and the hydrophobic core regions of both CH1 and CL. Expression levels of functional Fab fragments, denaturant-induced unfolding equilibria and circular dichroism spectroscopy were used to evaluate the relative stabilities of the wild-type and the mutant Fab fragments. The highest thermodynamic stability was reached through the mutation strategy, where the hydrophobicity and the packing density of the solvated hydrophobic cavity in the CH1/CL interface was increased by the replacement of the hydrophilic Thr178 in the CL domain by a more hydrophobic residue, valine or isoleucine. The midpoint of the transition curve from native to unfolded states of the protein, measured by fluorescence emission, occurred at concentrations of guanidine hydrochloride of 2.4 M and 2.6 M for the wild-type Fab and the most stable mutants, respectively. Our results illustrate that point mutations targeted to the CH1/ CL interface were advantageous for the overall thermodynamic stability of the Fab fragment.

L16 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:34781 CAPLUS Full-text
DOCUMENT NUMBER: 142:133074
TITLE: Modified antibody fragments with attached effector molecules and methods of production, and pharmaceutical composition thereof
INVENTOR(S): Heywood, Sam Philip; Humphreys, David Paul
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003171	A2	20050113	WO 2004-GB2871	20040701
WO 2005003171	A3	20050929		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2004253747	A1	20050113	AU 2004-253747	20040701
CA	2527866	A1	20050113	CA 2004-2527866	20040701
EP	1644413	A2	20060412	EP 2004-743217	20040701

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

JP	2008500945	T	20080117	JP 2006-516490	20040701
US	20070014802	A1	20070118	US 2006-562769	20060627

PRIORITY APPLN. INFO.: GB 2003-15457 A 20030701
WO 2004-GB2871 W 20040701

ED Entered STN: 14 Jan 2005

AB The disclosed invention relates to a new class of antibody fragments including antibody Fab and Fab' fragments in which the heavy (H) chain is not covalently bound to the light (L) chain and ≥2 effector mols. are attached to the fragment, of which at least one of said mols. is attached to a cysteine in the heavy or light chain constant region. The inventors describe the creation of a tri-PEGylated Fab' fragment by reducing the inter-chain disulfide of the antibody fragment g165 Fab' LC-C HC-C, hinge-CAA and attaching PEG mols. to the available thiols of the inter-chain cysteines of CL and CH1 and the hinge cysteine. The results indicate that there was no difference between Fab-PEG that have, or lack inter CL/CH1 disulfide bonds. Thus, novel PEGylated mols. of the invention can be produced more efficiently than PEGylated antibodies that contain CL/CH1 disulfide bond. Also, PEGylation of Fab' that lack the inter-chain disulfide bond has no adverse effects on the biol. activity or stability of Fab', thus making them useful therapeutic mols.

L16 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:34780 CAPLUS Full-text
DOCUMENT NUMBER: 142:112462
TITLE: Modified antibody fragments with attached effector mols., preparation, and uses thereof
INVENTOR(S): Humphreys, David Paul; Heywood, Sam Philip; Carrington, Bruce
PATENT ASSIGNEE(S): Celltech R & D Limited, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003170	A2	20050113	WO 2004-GB2870	20040701
WO 2005003170	A3	20050310		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,

BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2004253746	A1	20050113	AU 2004-253746	20040701
CA	2527003	A1	20050113	CA 2004-2527003	20040701
EP	1644044	A2	20060412	EP 2004-743216	20040701

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

JP	2007535472	T	20071206	JP 2006-516489	20040701
US	20070059301	A1	20070315	US 2005-562807	20051229
PRIORITY APPLN. INFO.:				GB 2003-15450 A	20030701
				WO 2004-GB2870 W	20040701

ED Entered STN: 14 Jan 2005

AB The present invention provides an antibody Fab or Fab' fragment to which at least one effector mol. is attached characterized in that the heavy chain in the fragment is not covalently bonded to the light chain and both the interchain cysteine of CL and the interchain cysteine of CH1 have been replaced with another amino acid. The methods provided here enable ≥1 effector mol(s). to be attached to cysteines in the antibody fragment, in particular to cysteines in the constant region and/or the hinge. The Fab' mols. discussed in the examples are gp165 Fab' which binds to a human cell surface receptor and g8516 which binds to human interleukin-1β. The Fab' fragments were PEGylated using non-thiol-containing reducing agents. The results also show on the example of the g8516-PEG that there are no differences between Fab' that have, or lack inter CL/CH1 disulfide bond. Thus, PEGylation of Fab' which lack the inter-chain disulfide bond has no adverse effect on the biol. activity or stability of Fab', making these mols. useful therapeutics.

L16 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:161999 CAPLUS Full-text
DOCUMENT NUMBER: 142:257312
TITLE: Bioanalytical reagents comprising element-coded affinity tags for detecting oxidized biomolecules and diagnostic use thereof
INVENTOR(S): Meares, Claude F.; Lebrilla, Carlito B.; Butlin, Nathaniel G.; Cheal, Sarah M.; Corneillie, Todd M.; Lee, Susan; Whetstone, Paul A.; Young, Nicolas L.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 84 pp., Cont.-in-part of U.S. Ser. No. 835,533.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050042695	A1	20050224	US 2004-854735	20040524
US 7267994	B2	20070911		
US 20050059100	A1	20050317	US 2004-835533	20040428
US 7214545	B2	20070508		
PRIORITY APPLN. INFO.:			US 2003-466529P P	20030428
			US 2003-495449P P	20030815
			US 2004-835533 A2	20040428

OTHER SOURCE(S): MARPAT 142:257312
ED Entered STN: 25 Feb 2005
AB The present invention provides bioanal. methods and reagents for the anal. of biomols., particularly, oxidized biomols., such as, e.g., proteins, nucleic

acids, lipids, and polysaccharides. The reagents comprise a chelating agent and a metal ion and are useful for fractionation and quant. (differential) profiling of biomols. in a complex mixture, and are referred to herein as "Element-Coded Affinity Tag" (ECAT) reagents. The ECAT reagents of the invention are useful as single tagging reagents, or as sets of two or more substantially similar but differentiable tagging reagents. The ECAT reagents can conveniently be used to detect, analyze, and identify multiple oxidized biomols. in a single sample, or the same oxidized biomol. in different samples. The ECAT reagents can also be used in diagnostic and therapeutic methods to detect levels of oxidized biomols. and patterns of biomol. oxidation in conjunction with disease progression and regression.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:390212 CAPLUS Full-text
DOCUMENT NUMBER: 140:390281
TITLE: Urea variants as affinity ligands for IgG
INVENTOR(S): Axen, Andreas; Baumann, Herbert; Carredano, Enrique; Groenberg, Anna; Steensma, Elles
PATENT ASSIGNEE(S): Amersham Biosciences Ab, Swed.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039765	A1	20040513	WO 2003-SE1434	20030912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003259007	A1	20040525	AU 2003-259007		20030912
US 20060014735	A1	20060119	US 2005-531783		20050418
PRIORITY APPLN. INFO.:			SE 2002-3226	A	20021031
			SE 2002-3878	A	20021220
			WO 2003-SE1434	W	20030912

OTHER SOURCE(S): MARPAT 140:390281
ED Entered STN: 13 May 2004
AB The present invention relates to an IgG-binding compound, which more specifically has affinity for human IgGs of k-type and functional derivs. thereof. More specifically, the compound according to the invention comprises an N,N-alkylated urea moiety located between an aromatic part and another part, which is a linear or cyclic substituted or unsubstituted aliphatic group. The compound binds to a pocket-shaped binding site present on all human IgGκ Fabs, which site is located between the two domains (CH1 and CL) of its constant part. Accordingly, the compound according to the invention is a ligand for human IgGs of .kappa.-type, and consequently, the invention also relates to a separation matrix for affinity chromatog., which matrix comprises said compound, as well as to other uses of the compound
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 36 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004272091 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15152083
TITLE: A novel and conserved pocket of human kappa-Fab fragments: design, synthesis, and verification of directed affinity ligands.
AUTHOR: Carredano Enrique; Baumann Herbert; Gronberg Anna; Norrman Nils; Glad Gunnar; Zou Jinyu; Ersoy Oguz; Steensma Elles; Axen Andreas
CORPORATE SOURCE: Amersham Biosciences R&D, Bjorkgatan 30, S-751 84 Uppsala, Sweden.
SOURCE: Protein science : a publication of the Protein Society, (2004 Jun) Vol. 13, No. 6, pp. 1476-88.
Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 3 Jun 2004
Last Updated on STN: 12 Jan 2005
Entered Medline: 11 Jan 2005
ED Entered STN: 3 Jun 2004
Last Updated on STN: 12 Jan 2005
Entered Medline: 11 Jan 2005
AB Antibodies of type IgG may be divided into two classes, called lambda or kappa, depending on the type of light chain. We have identified a conserved pocket between the two domains CH1 and CL of human IgG kappa-Fab , which is not present in the lambda type. This pocket was used as a target docking site with the purpose of exploring the possibilities of designing affinity ligands that could function as such even after immobilization to gel. The idea of the design arose mainly from the results of the saturated transfer difference (STD-NMR) screening of 46 compounds identified by means of virtual docking of 60 K diverse compounds from the Available Chemicals Directory (ACD). Surface plasmon resonance (SPR) was used as an alternative method to monitor binding in solution. A total of 24 compounds belonging to a directed library were designed, synthesized, and screened in solution. They consist essentially of an amino acid condensed to a N,N'-methylated phenyl urea. STD-NMR results suggest that a small hydrophobic side chain in the condensed amino acid promotes binding, whereas a hydroxyl-group-containing side chain implies absence of STD-NMR signals. Three compounds of the directed library were immobilized and evaluated as chromatographic probes. In one case, using D-Pro as the condensed amino acid, columns packed with ligand-coupled Sepharose (Amersham Biosciences) retained two different monoclonal samples of kappa-Fab fragments with different variable regions, whereas a sample of monoclonal lambda-Fab fragments was not retained under similar chromatographic conditions.

L16 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:624195 CAPLUS Full-text
DOCUMENT NUMBER: 141:241744
TITLE: Bivalent Fv Antibody Fragments Obtained by Substituting the Constant Domains of a Fab Fragment with Heterotetrameric Molybdopterin Synthase
AUTHOR(S): Petrov, Kliment; Dion, Michel; Hoffmann, Lionel; Dintinger, Thierry; Defontaine, Alain; Tellier, Charles
CORPORATE SOURCE: Faculte des Sciences et des Techniques, UMR-CNRS n°6204, Biotechnologie, Biocatalyse et Bioregulation, Nantes, 44322, Fr.
SOURCE: Journal of Molecular Biology (2004), 341(4), 1039-1048
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 04 Aug 2004
AB The antibody Fv fragment is the smallest functional unit of an antibody but for practical use, the VH/VL interface requires stabilization, which is usually accomplished by a peptide linker that joins the two variable domains to form a single chain Fv fragment (scFv). An alternative format to scFv is proposed that (i) allows stabilization of the Fv fragment, and (ii) restores the bivalency of the antibody as a pseudo-F(ab')2 format. This new antibody fragment was constructed by replacing the CH1 and CL domains of the Fab fragment with heterotetrameric molybdopterin synthase (MPTS). We found that this format, named MoaFv, improved significantly the cytoplasmic expression of the Fv as a soluble protein in BL21 or Origami Escherichia coli strains. This MoaFv format is expressed as a homogeneous heterotetrameric protein with a Mr value of 110 kDa containing two functional binding sites as revealed by active site titration In its native condition at 37° or in the presence of urea, this format was nearly as stable as the corresponding scFv, indicating that non-covalent interactions between the MPTS subunits can replace the covalent peptide linker in scFv. Finally, this MoaFv construct could be a useful format when bivalency is desirable to improve the functional avidity.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 11 OF 36 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004080769 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14693911
TITLE: Site-specific N-glycosylation of chicken serum IgG.
AUTHOR: Suzuki Noriko; Lee Yuan C
CORPORATE SOURCE: Department of Biology, Johns Hopkins University, Baltimore, MD 21218, USA.. nrsuzuki@jhu.edu
CONTRACT NUMBER: DK09970 (United States NIDDK)
SOURCE: Glycobiology, (2004 Mar) Vol. 14, No. 3, pp. 275-92.
Electronic Publication: 2003-12-23.
Journal code: 9104124. ISSN: 0959-6658.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 19 Feb 2004
Last Updated on STN: 7 Oct 2004
Entered Medline: 6 Oct 2004
ED Entered STN: 19 Feb 2004
Last Updated on STN: 7 Oct 2004
Entered Medline: 6 Oct 2004
AB Avian serum immunoglobulin (IgG or IgY) is functionally equivalent to mammalian IgG but has one additional constant region domain (CH2) in its heavy (H) chain. In chicken IgG, each H-chain contains two potential N-glycosylation sites located on CH2 and CH3 domains. To clarify characteristics of N-glycosylation on avian IgG, we analyze N-glycans from chicken serum IgG by derivatization with 2-aminopyridine (PA) and identified by HPLC and MALDI-TOF-MS. There were two types of N-glycans: (1) high-mannose-type oligosaccharides (monoglucosylated 26.8%, others 10.5%) and (2) biantennary complex-type oligosaccharides (neutral, 29.9%; monosialyl, 29.3%; disialyl, 3.7%) on molar basis of total N-glycans. To investigate the site-specific localization of different N-glycans, chicken serum IgG was digested with papain and separated into Fab [containing variable regions (VH + VL) + CH1 + CL] and Fc (containing CH3 + CH4) fragments. Con A stained only Fc (CH3 + CH4) and RCA-I stained only Fab fractions, suggesting that high-mannose-type

oligosaccharides were located on Fc (CH3 + CH4) fragments, and variable regions of Fab contains complex-type N-glycans. MS analysis of chicken IgG-glycopeptides revealed that chicken CH3 domain (structurally equivalent to mammalian CH2 domain) contained only high-mannose-type oligosaccharides, whereas chicken CH2 domain contained only complex-type N-glycans. The N-glycosylation pattern on avian IgG is more analogous to that in mammalian IgE than IgG, presumably reflecting the structural similarity to mammalian IgE.

L16 ANSWER 12 OF 36 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003441861 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14500870
TITLE: Interaction between the antigen and antibody is controlled by the constant domains: normal mode dynamics of the HEL-HyHEL-10 complex.
AUTHOR: Adachi Masaaki; Kurihara Youji; Nojima Hiroyuki; Takeda-Shitaka Mayuko; Kamiya Kenshu; Umeyama Hideaki
CORPORATE SOURCE: School of Pharmaceutical Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8641, Japan.
SOURCE: Protein science : a publication of the Protein Society, (2003 Oct) Vol. 12, No. 10, pp. 2125-31.
Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 23 Sep 2003
Last Updated on STN: 20 May 2004
Entered Medline: 19 May 2004
ED Entered STN: 23 Sep 2003
Last Updated on STN: 20 May 2004
Entered Medline: 19 May 2004
AB The antigen binding fragment (Fab) of a monoclonal antibody (HyHEL-10) consists of variable domains (Fv) and constant domains (CL-CH1). Normal modes have been calculated from the three-dimensional structures of hen egg lysozyme (HEL) with Fab, those of HEL with Fv, and so on. Only a small structural change was found between HEL-Fab and HEL-Fv complexes. However, HEL-Fv had a one order of magnitude lower dissociation constant than HEL-Fab. The Calpha fluctuations of HEL-Fab differed from those of HEL-Fv with normal mode calculation, and the dynamics can be thought to be related to the protein-protein interactions. CL-CH1 may have influence not only around local interfaces between CL-CH1 and Fv, but also around the interacting regions between HEL and Fv, which are longitudinally distant. Eighteen water molecules were found in HEL-Fv around the interface between HEL and Fv compared with one water molecule in HEL-Fab. These solvent molecules may occupy the holes and channels, which may occur due to imperfect complementarity of the complex. Therefore, the suppression of atomic vibration around the interface between Fv and HEL can be thought to be related to favorable and compact interface formation by complete desolvation. It is suggested that the ability to control the antigen-antibody affinity is obtained from modifying the CL-CH1. The second upper loop in the constant domain of the light chain (UL2-CL), which is a conserved gene in several light chains, showed the most remarkable fluctuation changes. UL2-CL could play an important role and could be attractive for modification in protein engineering.

L16 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:31655 CAPLUS Full-text
DOCUMENT NUMBER: 136:97299

TITLE: Methods of producing multispecific heterodimeric fusion protein diabodies and uses in diagnosis and therapy
INVENTOR(S): Mertens, Nico; Grooten, Johan
PATENT ASSIGNEE(S): Vlaams Interuniversitair Instituut Voor Biotechnologie Vzw, Belg.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002781	A1	20020110	WO 2001-EP7557	20010629

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2410551	A1	20020110	CA 2001-2410551	20010629
AU 2001070609	A	20020114	AU 2001-70609	20010629
EP 1294904	A1	20030326	EP 2001-949457	20010629

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 20040220388	A1	20041104	US 2002-312923	20021227

PRIORITY APPLN. INFO.:

EP 2000-202306	A	20000630
WO 2001-EP7557	W	20010629

ED Entered STN: 11 Jan 2002
AB The invention discloses the production of bispecific or multispecific, bi- or tetravalent antibodies using recombinant DNA methods and recombinant production methods. The resulting antibody consists of one or two diabody mols. that are heterodimerized by creating a fusion protein with the CL and CH1 Ig constant domains. In particular, each of the chains of the novel heterodimer contains a fusion protein that consists of one or more diabody chains that are coupled to the CL or the CH1 constant Ig domain and forms the formula VH(A)-VL(B)-CL:VH(B)-VL(A)-CH1, where the diabody chains can either be fused at the C-terminus or N-terminus of the Ig constant domain and the order of VH-VL can be reversed. The invention further discloses methods for making these novel heterodimers, DNA comprising genes encoding these novel fusion proteins, transformed host cells, and uses of the fusion proteins for diagnosis and therapy.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 6
ACCESSION NUMBER: 2001:491551 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100491551
TITLE: Helix-stabilized Fv (hsFv) antibody fragments: Substituting the constant domains of a Fab fragment for a heterodimeric coiled-coil domain.
AUTHOR(S): Arndt, Katja M.; Muller, Kristian M.; Pluckthun, Andreas [Reprint author]
CORPORATE SOURCE: Biochemisches Institut, Universitat Zurich, Winterthurerstr. 190, 8057, Zurich, Switzerland
plueckthun@biocfebs.unizh.ch
SOURCE: Journal of Molecular Biology, (7 September, 2001) Vol. 312, No.

1, pp. 221-228. print.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002
ED Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002
AB Antibody Fv fragments would in principle be useful for a variety of biotechnological applications because of their small size and the possibility to produce them in relatively large amounts in recombinant form; however, their limited stability is a drawback. To solve this problem, both domains are usually fused via a peptide linker to form a single-chain Fv (scFv) fragment, but in some cases this leads to a dimerization. We present an alternative format for stabilizing antibody Fv fragments. The CH1 and CL domain of the Fab fragment were replaced with a heterodimeric coiled coil (WinZip-A2B1), which had previously been selected using a protein-fragment complementation assay in Escherichia coli. This new anti-body format was termed helix-stabilized Fv fragment (hsFv), and was compared to the corresponding Fv, Fab and single-chain Fv format. Bacterial growth and expression of the hsFv was significantly improved compared to the Fab fragment. The hsFv fragment formed a heterodimer of heavy and light chain with the expected molecular mass, also under conditions where the scFv fragment was predominantly dimeric. The hsFv fragment was significantly more stable than the Fv fragment, and nearly as stable as the scFv fragment under the conditions used (80 nM protein concentration). Thus, the format of a helix-stabilized Fv (hsFv) fragment can be a useful alternative to existing recombinant antibody formats, especially in cases where poor expression of Fab fragments or multimerization of scFv fragments is a problem.

L16 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:475568 CAPLUS Full-text
DOCUMENT NUMBER: 135:44981
TITLE: New recombinant bi- and trispecific antibody derivatives
AUTHOR(S): Mertens, Nico; Schoonjans, Reinilde; Willems, An; Schoonooghe, Steve; Leoen, Jannick; Grooten, Johan
CORPORATE SOURCE: Molecular Immunology Unit, Department of Molecular Biology, Flanders Interuniversity Institute of Biotechnology (VIB), Ghent University, Ghent, B-9000, Belg.
SOURCE: Focus on Biotechnology (2001), 1(Novel Frontiers in the Production of Compounds for Biomedical Use), 195-208
CODEN: FBOIAM
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 03 Jul 2001
AB Bispecific antibodies (BsAb) are promising therapeutic tools in tomorrow's medicine. When constructing BsAbs, the final mol. size should be large enough to avoid rapid renal clearing, but small enough to allow efficient tissue distribution. In order to produce such intermediate sized BsAb, a good heterodimerization technique will improve existing production methods. When considering recombinant expression of BsAbs, the heterodimerization motif can be incorporated into the mol. Recombinant BsAb can e.g. be made by fusing single chain variable fragments (scFv) to a heterodimerization domain. We compared the efficiency of the isolated CL and CH1 constant domains with complete Fab chains to drive heterodimerization of BsAbs in mammalian cells. We found that the isolated CL:CH1 domain interaction was inefficient for secretion of heterodimers. However, when the complete Fab chains were used, secretion of a heterodimerized bispecific antibody was successful. By C-

terminal fusion of scFv mols. to the Fd- and the L-chains efficient heterodimerization in mammalian cells was obtained and a novel intermediate sized, disulfide stabilized BsAb could be efficiently produced. Since the Fab chain encodes a binding specificity on its own, bispecific (BsAb) or trispecific (TsAb) antibodies can be made. This gave rise to disulfide stabilized Fab-scFv BsAb (Bibody) or Fab-(scFv)2 TsAb (Tribody) of intermediate mol. size. Heterodimerization of the L and Fd-containing fusion proteins was very efficient, and up to 90% of all secreted antibody fragments was in the desired heterodimerized format. All building blocks remained functional in the fusion product, and the bispecific character of the mols. as well as the functionality was demonstrated. Due to the high heterodimerization efficiency, the ease of purification of the desired product from byproducts and the lack of post-production processing, this method for producing bi- or trispecific antibodies in mammalian cells could become a method of choice for the production of intermediate sized trispecific antibodies, BsAb with monovalent or bivalent binding for one antigen, or immunoconjugates.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 36 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2001396164 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11337278

TITLE: A new model for intermediate molecular weight recombinant bispecific and trispecific antibodies by efficient heterodimerization of single chain variable domains through fusion to a Fab-chain.

AUTHOR: Schoonjans R; Willems A; Schoonooghe S; Leoen J; Grooten J; Mertens N

CORPORATE SOURCE: Department of Molecular Biology, Molecular Immunology Unit, Flanders Interuniversity, Institute for Biotechnology (VIB), University of Ghent, K.L. Ledeganckstraat 35, B-9000 Ghent, Belgium.

SOURCE: Biomolecular engineering, (2001 Jun) Vol. 17, No. 6, pp. 193-202.

Journal code: 100928062. ISSN: 1389-0344.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200107

ENTRY DATE: Entered STN: 16 Jul 2001
Last Updated on STN: 16 Jul 2001
Entered Medline: 12 Jul 2001

ED Entered STN: 16 Jul 2001
Last Updated on STN: 16 Jul 2001
Entered Medline: 12 Jul 2001

AB Due to their specificity and versatility in use, bispecific antibodies (BsAbs) are promising therapeutic tools in tomorrow's medicine, provided sufficient BsAb can be produced. Expression systems favoring efficient heterodimerization of intermediate-sized bispecific antibodies will significantly improve existing production methods. Recombinant BsAb can be made by fusing single chain variable fragments (scFv) to a heterodimerization domain. We compare the efficiency of the isolated CL and CH1 constant domains with complete Fab chains to drive heterodimerization of BsAbs in mammalian cells. We found that the isolated CL:CH1 domain interaction was inefficient for secretion of heterodimers. However, when the complete Fab chains were used, secretion of a heterodimerized bispecific antibody was successful. Since the Fab chain encodes a binding specificity on its own, bispecific (BsAb) or trispecific (TsAb) antibodies can be made by C-terminal fusion of scFv molecules to the L or Fd Fab chains. This gave rise to disulphide

stabilized Fab-scFv BsAb (Bibody)or Fab-(scFv)2 TsAb (Tribody) of intermediate molecular size. Heterodimerization of the L and Fd-containing fusion proteins was very efficient, and up to 90% of all secreted antibody fragments was in the desired heterodimerized format. All building blocks remained functional in the fusion product, and the bispecific character of the molecules as well as the immunological functionality was demonstrated.

L16 ANSWER 17 OF 36 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001091148 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11120833
TITLE: Fab chains as an efficient heterodimerization scaffold for the production of recombinant bispecific and trispecific antibody derivatives.
AUTHOR: Schoonjans R; Willems A; Schoonooghe S; Fiers W; Grooten J; Mertens N
CORPORATE SOURCE: Molecular Immunology Unit, Department of Molecular Biology, Flanders Interuniversity Institute for Biotechnology, Ghent University, Ghent, Belgium.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2000 Dec 15) Vol. 165, No. 12, pp. 7050-7.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 25 Jan 2001
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 25 Jan 2001
AB Due to their multispecificity and versatility, bispecific Abs (BsAbs) are promising therapeutic tools in tomorrow's medicine. Especially intermediate-sized BsAbs that combine body retention with tissue penetration are valuable for therapy but necessitate expression systems that favor heterodimerization of the binding sites for large-scale application. To identify heterodimerization domains to which single-chain variable fragments (scFv) can be fused, we compared the efficiency of heterodimerization of CL and CH1 constant domains with complete L and Fd chains in mammalian cells. We found that the isolated CL:CH1 domain interaction was inefficient for secretion of heterodimers. However, when the complete L and Fd chains were used, secretion of L:Fd heterodimers was highly successful. Because these Fab chains contribute a binding moiety, C-terminal fusion of a scFv molecule to the L and/or Fd chains generated BsAbs or trispecific Abs (TsAbs) of intermediate size (75-100 kDa). These disulfide-stabilized bispecific Fab-scFv ("bibody") and trispecific Fab-(scFv)(2) ("tribody") heterodimers represent up to 90% of all secreted Ab fragments in the mammalian expression system and possess fully functional binding moieties. Furthermore, both molecules recruit and activate T cells in a tumor cell-dependent way, whereby the trispecific derivative can exert this activity to two different tumor cells. Thus we propose the use of the disulfide-stabilized L:Fd heterodimer as an efficient platform for production of intermediate-sized BsAbs and TsAbs in mammalian expression systems.

L16 ANSWER 18 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 9
ACCESSION NUMBER: 1999:227809 BIOSIS Full-text

DOCUMENT NUMBER: PREV199900227809
TITLE: Generation and characterization of a novel single-gene-encoded single-chain immunoglobulin molecule with antigen binding activity and effector functions.
AUTHOR(S): Lee, Hyun-Sil; Shu, Liming; De Pascalis, Roberto; Giuliano, Mariateresa; Zhu, Mingzhu; Padlan, Eduardo A.; Horan Hand, Patricia; Schlom, Jeffrey; Hong, Hyo Jeong; Kashmiri, S. V. S. [Reprint author]
CORPORATE SOURCE: Laboratory of Tumor Immunology and Biology, National Cancer Institute, Bethesda, MD, 20892, USA
SOURCE: Molecular Immunology, (Jan., 1999) Vol. 36, No. 1, pp. 61-71. print.
CODEN: MOIMD5. ISSN: 0161-5890.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999
ED Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999
AB Monoclonal antibody (MAb) CC49 is a murine IgG1 that reacts with tumor-associated glycoprotein (TAG)-72, a pancarcinoma antigen. Clinical trials using radiolabeled CC49 for diagnostic imaging have demonstrated specific localization of more than 90% of carcinomas. The feasibility of adopting in vivo gene inoculation methods for antibody-based immunotherapy requires introduction and expression of two genes, encoding immunoglobulin (Ig) heavy and light chains, in a single cell to generate a functional antibody. To circumvent the problems inherent in this approach, we have constructed a single-gene encoding a single-chain immunoglobulin (SCIg) that, unlike previously developed SCIgs, contains all IgG domains. To construct the novel SCIg, the carboxyl end of the constant region of the chimeric (c) CC49 kappa chain is joined, via a 30 residue Gly-Ser linker peptide, to the amino terminus of the CC49 heavy chain. To our knowledge, neither a linker peptide this long nor a linkage between the constant light (CL) and variable heavy domains has been reported previously. Transfectomas developed by introducing the expression construct of the amplifiable gene in dihydrofolate reductase-deficient Chinese hamster ovary (CHO dhfr-) cells secrete a 160 kDa homodimeric molecule, SCIgcCC49. The in vitro antigen binding properties of SCIgcCC49 are comparable to those of cCC49 and SCIgcCC49DELTACH1, a single-chain Ig deficient in constant heavy chain-1 (CH1) and CL domains. The antibody-dependent cellular cytotoxicity (ADCC) of SCIgcCC49 and cCC49 were also comparable. This single-gene approach for generating an immunoglobulin molecule may facilitate in vivo gene inoculation as well as ex vivo transfection of patients' cultured tumor-infiltrating lymphocytes for immunotherapy protocols for a variety of diseases, including cancer.

L16 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:224843 CAPLUS Full-text
DOCUMENT NUMBER: 128:293691
ORIGINAL REFERENCE NO.: 128:58183a,58186a
TITLE: Progress in programming antibody fragments to crystallize
AUTHOR(S): Edmundson, Allen B.; Borrebaeck, Carl A. K.
CORPORATE SOURCE: Oklahoma Medical Research Foundation, Oklahoma City, OK, 73104, USA
SOURCE: Immunotechnology (1998), 3(4), 309-317
CODEN: IOTEER; ISSN: 1380-2933
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 22 Apr 1998

AB A review and discussion with 14 refs. Discussed are: bilateral formation of β-pleated sheets across 2-fold axes; formation of β-pleated sheets by CL or CH1, but not both; cross-mol. β-sheet produced by κ-type VL domains; structural features favoring β-sheet formation; cross-mol. hydrogen bonding in crystals of the Mcg dimer; hydrogen bonding across 2-fold axes in the Mcg κ Hud hybrid; intermol. hydrogen bonding between CL and CH1 in B7-15A2; hydrogen bonding between antiparallel CH1 domains in Fab new; hydrogen bonding between symmetry-related κ-type VL domains; programming crystallization into the design of some Fabs; exceptions to the rules: CL domains of κ-type L chains; structures of turns between 3-2 and 3-3 in the B7-15A2 Fab; structure of the κ chain loop between β-strands 3-2 and 3-3; and usage of amino acid triads in CL-CL or CL-CH1 packing.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 36 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 10
ACCESSION NUMBER: 1998:136360 BIOSIS Full-text
DOCUMENT NUMBER: PREV199800136360
TITLE: The first constant domain (CH1 and CL) of an antibody used as heterodimerization domain for bispecific miniantibodies.
AUTHOR(S): Mueller, Kristian M.; Arndt, Katja M.; Strittmatter, Wolfgang; Pluckthun, Andreas [Reprint author]
CORPORATE SOURCE: Biochemisches Inst., Univ. Zurich, Winterthurerstr. 190, CH-8057 Zurich, Switzerland
SOURCE: FEBS Letters, (Jan. 20, 1998) Vol. 422, No. 2, pp. 259-264. print.
CODEN: FEBLAL. ISSN: 0014-5793.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Mar 1998
Last Updated on STN: 20 Mar 1998
ED Entered STN: 20 Mar 1998
Last Updated on STN: 20 Mar 1998
AB Bispecific miniantibodies were constructed by genetically fusing the CH1 domain of an IgG1 to the C-terminus of a single-chain Fv fragment (scFv-425), specific for the EGF receptor, and fusing the CL domain of a kappa light chain to the C-terminus of a scFv specific for CD2 (scFv-M1). An efficient dicistronic gene arrangement for functional expression in Escherichia coli was constructed. Immunoblots demonstrated correct domain assembly and the formation of the natural CH1-CL disulfide bridge. Gel filtration confirmed the correct size, sandwich ELISAs demonstrated bispecific functionality, and SPR biosensor measurements determined binding to EGF-R in comparison to bivalent constructs. Bispecific anti-EGF-R/anti-CD2 miniantibodies are candidates for the immunotherapy of cancer.

L16 ANSWER 21 OF 36 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2003009323 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12515168
TITLE: Construction and screening of type 1 human immunodeficiency virus specific phage antibodies combinatorial library.
AUTHOR: He Y; Wang X; Liu S
CORPORATE SOURCE: Research Center of Virology, Beijing Ditan Hospital, Beijing 100011.
SOURCE: Zhonghua shi yan he lin chuang bing du xue za zhi = Zhonghua shiyan he linchuang bingduxue zazhi = Chinese journal of experimental and clinical virology, (1998 Mar) Vol. 12, No. 1, pp. 33-7.
Journal code: 9602873. ISSN: 1003-9279.

PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 8 Jan 2003
Last Updated on STN: 4 Feb 2003
Entered Medline: 3 Feb 2003
ED Entered STN: 8 Jan 2003
Last Updated on STN: 4 Feb 2003
Entered Medline: 3 Feb 2003
AB Human monoclonal antibodies to type 1 immunodeficiency virus (HIV-1) gp120 were generated from phage antibody combinatorial library. METHODS: The human immunoglobulin heavy chain Fd and light chain k genes were amplified by half-nested PCR from PBMC of patient infected with HIV. Phage antibody combinatorial library was constructed with the Fd and k chain genes using Pcomb3 as vector. The affinity selection and ELISA were adopted for generating specific phage antibodies. Partial DNA of a positive clone was sequenced and its soluble Fab was expressed in E coli. HIV-1 specific phage antibodies combinatorial library were constructed using the Fd and k genes and Pcomb3 vector. The library capacity was about 1.95 x 10(7). The specific phage antibodies were highly enriched after three rounds of biopanning selection against HIV-1 gp120 and 32% positive clones were detected by ELISA screening. DNA fragment coding for CH1 and CL derived from a positive clone was sequenced and its product was successfully expressed as soluble Fab which was specific for HIV-1 gp120. The HIV-1 specific phage antibody combinatorial library, and human monoclonal antibodies to HIV-1 gp120 have been used as tools for screening of neutralizing antibody to HIV-1, and the methods seem to be very crucial and applicable.

L16 ANSWER 22 OF 36 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 1996214983 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8621386
TITLE: Comparative properties of the single chain antibody and Fv derivatives of mAb 4-4-20. Relationship between interdomain interactions and the high affinity for fluorescein ligand.
AUTHOR: Mallender W D; Carrero J; Voss E W Jr
CORPORATE SOURCE: Department of Microbiology, University of Illinois, Urbana, 61801, USA.
CONTRACT NUMBER: RR03155-01 (United States NCRR)
SOURCE: The Journal of biological chemistry, (1996 Mar 8) Vol. 271, No. 10, pp. 5338-46.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 27 Jun 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 20 Jun 1996
ED Entered STN: 27 Jun 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 20 Jun 1996

AB Recombinant Fv derivative of the high affinity murine anti-fluorescein monoclonal antibody 4-4-20 was constructed and expressed in high yields, relative to the single chain antibody (SCA) derivative (2 3-fold), in Escherichia coli. Both variable heavy (VH) and variable light (VL) domains, that accumulated as insoluble inclusion bodies, were isolated, denatured, mixed, refolded, and affinity-purified to yield active Fv 4-4-20. Affinity-purified Fv 4-4-20 showed identical ligand binding properties compared with the SCA construct, both were slightly lower than the affinities expressed by Fab or IgG 4-4-20. Proper protein folding was shown to be domain-independent by in vitro mixing of individually refolded variable domains to yield functional Fv protein. In solid phase and solution phase assays, Fv 4-4-20 closely approximated the SCA derivative in terms of both idiotype and metatype, confirming identical active site structures and conformations. The equilibrium dissociation constant (Kd) for the VL/VH association (1.43 x 10(-7) M), which was determined using the change in fluorescein spectral properties upon ligand binding, was relatively low considering the high affinity displayed by the Fv protein for fluorescein (Kd, 2.9 x 10(-10) M). Thus, domain-domain stability in the Fv and SCA 4-4-20 proteins cannot be the sole cause of reduced affinity (2-3-fold) for fluorescein as compared with the Fab or IgG form of 4-4-20. With their identical ligand binding and structural properties, the decreased SCA or Fv affinity for fluorescein must be an ultimate consequence of deletion of the CH1 and CL constant domains. Collectively, these results verify the importance of constant domain interactions in antibody variable domain structure-function analyses and future antibody engineering endeavors.

L16 ANSWER 23 OF 36 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1996266491 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8683596
TITLE: X-ray structure of the uncomplexed anti-tumor antibody BR96 and comparison with its antigen-bound form.
AUTHOR: Sheriff S; Chang C Y; Jeffrey P D; Bajorath J
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08543-4000, USA.
SOURCE: Journal of molecular biology, (1996 Jun 28) Vol. 259, No. 5, pp. 938-46.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 28 Aug 1996
Last Updated on STN: 28 Aug 1996
Entered Medline: 20 Aug 1996
ED Entered STN: 28 Aug 1996
Last Updated on STN: 28 Aug 1996
Entered Medline: 20 Aug 1996
AB The X-ray structure of the uncomplexed human chimeric Fab' of the anti-tumor antibody BR96 has been determined at 2.6 A resolution. The structure has been compared with Lewis Y antigen-complexed structures of BR96 which were determined previously. The comparison reveals segmental motions and/or conformational rearrangements of three CDR loops (L1, L3, and H2), whereas CDR H3 does not undergo changes upon complexation despite its significant main-chain contacts to the carbohydrate antigen. In light of the uncomplexed chimeric Fab' structure reported here, the previously observed high mobility of the CL:CH1 domains of the complexed chimeric BR96 Fab is rationalized as a "swinging" motion approximately about the axis of the elbow bend.

L16 ANSWER 24 OF 36 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1996317115 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8743296
TITLE: Cloning and expression of cDNAs encoding the variable domains of the antibreast carcinoma antibody Mc5.
AUTHOR: Christian R B; Couto J R; Peterson J A; Ceriani R L
CORPORATE SOURCE: Cancer Research Fund of Contra Costa, Walnut Creek, California 94596, USA.
SOURCE: Hybridoma, (1996 Apr) Vol. 15, No. 2, pp. 155-8.
Journal code: 8202424. ISSN: 0272-457X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-S83372; GENBANK-S83373
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19 Dec 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 6 Nov 1996
ED Entered STN: 19 Dec 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 6 Nov 1996
AB Mc5, a murine monoclonal antibody that binds to human breast epithelial mucin (BEM), has been shown to be a promising reagent in the diagnosis of breast cancer. We have cloned cDNAs encoding both variable regions of Mc5 (VL and VH) as well as the CL and CH1 constant regions. Mc5 is an IgG1, kappa antibody. We have constructed an IgG1, kappa human/mouse chimeric antibody (by inserting the murine VH and VL-encoding cDNAs into plasmids encoding human constant domains), and expressed it in SP2/0-Ag14 mouse myeloma cells. The affinity of chimeric Mc5 (chMc5) for BEM is 4.4 x 10(8) M-1. Mc5 binds BEM with an affinity constant of 2.8 x 10(8) M-1. Purified chMc5 and purified Mc5 gave similar competition curves when tested against either 125I-labeled Mc5 or 125I-labeled chMc5 for binding to BEM in a competition radioimmunodetection format. Additionally, chMc5 used in breast carcinoma tissue staining stained as well as the original Mc5.

L16 ANSWER 25 OF 36 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1992153678 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1739617
TITLE: Human/mouse chimeric antibodies show low reactivity with human anti-murine antibodies (HAMA).
AUTHOR: Hosono M; Endo K; Sakahara H; Watanabe Y; Saga T; Nakai T; Kawai C; Matsumori A; Yamada T; Watanabe T; +
CORPORATE SOURCE: Department of Nuclear Medicine, Kyoto University Hospital, Japan.
SOURCE: British journal of cancer, (1992 Feb) Vol. 65, No. 2, pp. 197-200.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 10 Apr 1992
Last Updated on STN: 10 Apr 1992
Entered Medline: 24 Mar 1992
ED Entered STN: 10 Apr 1992
Last Updated on STN: 10 Apr 1992

Entered Medline: 24 Mar 1992

AB Human anti-murine antibody (HAMA) response is a serious problem in the repeated infusion of murine monoclonal antibodies (MoAbs). HAMA positive sera were obtained from seven patients with colorectal cancer, pancreas cancer, malignant melanoma or myocardial infarction who had previously received radiolabelled MoAbs. The nature of HAMA was analysed using size exclusion high performance liquid chromatography (HPLC) after incubating with radiolabelled MoAbs including IgG, Fab or human/mouse chimeric Absolute Immune complexes composed of HAMA and MoAbs were formed. The percentage of radioactivity with a high molecular weight was related to HAMA levels determined by enzyme linked immunosorbent assay. Most radioactivity present in immune complex shifted to the antibody fraction after the addition of normal murine serum. All of seven sera were reactive with all four murine IgGs and this suggests that HAMA in these patients recognised the constant region of MoAbs. In one patient, HAMA was considered to recognise the variable region and to be anti-idiotypic. There was no significant binding with human/mouse chimeric Abs in any HAMA positive serum, although five out of seven patients were reactive with murine MoAb Fab, indicating that HAMA was composed of Abs responsive to the CH1 or CL region of murine IgG. These results suggest that (1) HAMA was composed of Ab responsive to Fc portion and/or CH1 or CL region of murine IgG, and (2) human/mouse chimeric Abs look promising in the repeated infusion of MoAb in HAMA positive patients.

L16 ANSWER 26 OF 36 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1992015212 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1920408
TITLE: 2.9 A resolution structure of an anti-dinitrophenyl-spin-label monoclonal antibody Fab fragment with bound hapten.
AUTHOR: Brunger A T; Leahy D J; Hynes T R; Fox R O
CORPORATE SOURCE: Howard Hughes Medical Institute, Yale University, New Haven, CT 06511.
SOURCE: Journal of molecular biology, (1991 Sep 5) Vol. 221, No. 1, pp. 239-56.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 24 Jan 1992
Entered Medline: 25 Oct 1991

ED Entered STN: 24 Jan 1992
Last Updated on STN: 24 Jan 1992
Entered Medline: 25 Oct 1991

AB The crystal structure of the Fab fragment of the murine monoclonal anti-dinitrophenyl-spin-label antibody AN02 complexed with its hapten has been solved at 2.9 A resolution using a novel molecular replacement method. Prior to translation searches, a large number of the most likely rotation function solutions were subjected to a rigid body refinement against the linear correlation coefficient between intensities of observed and calculated structure factors. First, the overall orientation of the search model and then the orientations and positions of the four Fab domains (VH, VL, CH1 and CL) were refined. This procedure clearly identified the correct orientation of the search model. The refined search model was then subjected to translation searches which unambiguously determined the enantiomer and position in the unit cell of the crystal. The successful search model was

refined 2.5 A crystal structure of the Fab fragment of HyHel-5 from which non-matching residues in the variable domains had been removed. HyHel-5 is a murine monoclonal antibody whose heavy and light chains are of the same subclass (gamma 1, kappa, respectively) as AN02. After molecular replacement the structure of the AN02 Fab has been refined using simulated annealing in combination with model building and conjugate gradient refinement to a current crystallographic R-factor of 19.5% for 12,129 unique reflections between 8.0 and 2.9 A. The root-mean-square (r.m.s.) deviation from ideal bond lengths is 0.014 A, and the r.m.s. deviation from ideal bond angles is 3.1 degrees. The electron density reveals the hapten sitting in a pocket formed by the loops of the complementarity determining region. The dinitrophenyl ring of the hapten is sandwiched between the indole rings of Trp96 of the heavy-chain and Trp91 of the light-chain. The positioning of the hapten and general features of the combining site are in good agreement with the results of earlier nuclear magnetic resonance experiments.

L16 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:421925 CAPLUS Full-text
DOCUMENT NUMBER: 113:21925
ORIGINAL REFERENCE NO.: 113:3789a,3792a
TITLE: Molecular-replacement structure determination of two different antibody:antigen complexes
AUTHOR(S): Sheriff, Steven; Padlan, Eduardo A.; Cohen, Gerson H.; Davies, David R.
CORPORATE SOURCE: Natl. Inst. Diabetes, Dig. Kidney Dis., Bethesda, MD, 20892, USA
SOURCE: Acta Crystallographica, Section B: Structural Science (1990), B46(3), 418-25
CODEN: ASBSDK; ISSN: 0108-7681
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Jul 1990
AB Mol. replacement was used to determine the structures of two antibody:antigen complexes, HyHEL-5 Fab:lysozyme and HyHEL-10 Fab:lysozyme by orienting and locating the CL:CH1 domains, Fv and lysozyme. The model of McPC603 was used as probe for the CL:CH1 domains and Fv. In HyHEL-5 Fab:lysozyme, there were two closely related crystal forms and the top peak in the rotation function was correct in five out of six cases (two crystals and three probes). The top peak in the Crowther-Blow translation function was also correct in five out of six cases. The program BRUTE Fujinaga and Read (1987) was used to put together the three pieces and thereby solve the relative origin problem in space group P21. In HyHEL-10 Fab:lysozyme the top peak in the rotation function was correct for the FV and lysozyme, but even with an appropriate model (the CL:CH1 domains of HyHEL-5) it was no better than the seventh peak (72% of the top peak) for CL:CH1. In the Crowther-Blow translation function, the top peaks were correct on two of three Harker sections for the Fv domains and lysozyme. The Crowther-Blow translation function was unable to locate CL:CH1, when using McPC603 CL:CH1 as the probe; however, when HyHEL-5 CL:CH1 was used, the top peak in all three sections was correct.

L16 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:196572 CAPLUS Full-text
DOCUMENT NUMBER: 112:196572
ORIGINAL REFERENCE NO.: 112:33221a,33224a
TITLE: Domain-modified constant region antibodies
INVENTOR(S): Morrison, Sherie L.; Oi, Vernon T.
PATENT ASSIGNEE(S): Columbia University, USA; Becton Dickinson and Co.
SOURCE: Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 327378	A1	19890809	EP 1989-301052	19890203
EP 327378	B1	19961211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
WO 8907142	A1	19890810	WO 1989-US297	19890124
W: JP				
JP 02503056	T	19900927	JP 1989-502277	19890124
JP 3095168	B2	20001003		
AU 8928942	A	19890810	AU 1989-28942	19890131
AU 637313	B2	19930527		
AT 146221	T	19961215	AT 1989-301052	19890203
CA 1340863	C	19991228	CA 1989-590118	19890203
PRIORITY APPLN. INFO.:			US 1988-152741 A	19880205
			WO 1989-US297 W	19890124

ED Entered STN: 26 May 1990

AB An antibody having ≥1 binding site region and a domain-modified constant region is provided. The domain modification is either a substitution of, an insertion of, or a deletion of substantially all of the amino acids of ≥1 of the domains of a constant region: CL, CH1, hinge, CH2 CH3 or CH4. The functional properties of the domain-modified constant region antibodies are selected to enhance the desired biol. functions for a particular application. Antibody constant-region domains can be eliminated, inserted, or substituted for (exchanged) by a domain of a different isotype or Ig class or from the light chain. The substituted or inserted domain can be from the same antibody or from another antibody of the same animal, the same species of animal, or a different species of animal. In this way, the functional properties of the biol. mol. can be optimized for the desired application. DNA constructs encoding domain-modified constant regions, constructs encoding complete constant-region-domain-modified antibodies, and cells expressing such antibodies are also provided. A protein prepared from vector 1654 having a chimeric gene encoding γ3 CH1 and hinge and γ2 CH2 and CH3 domains had the Fc receptor binding activity of IgG2. It did not bind the Fc receptor of human monocyte cell lines.

L16 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:495849 CAPLUS Full-text
DOCUMENT NUMBER: 113:95849
ORIGINAL REFERENCE NO.: 113:16171a,16174a
TITLE: Immunochemical and crystallographic studies of antibody D1.3 in its free, antigen-liganded, and idiotope-bound states
AUTHOR(S): Bentley, G. A.; Bhat, T. N.; Boulot, G.; Fischmann, T.; Navaza, J.; Poljak, R. J.; Riottot, M. M.; Tello, D.
CORPORATE SOURCE: Dep. Immunol., Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Cold Spring Harbor Symposia on Quantitative Biology (1989), 54(1), 239-45
CODEN: CSHSAZ; ISSN: 0091-7451
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 16 Sep 1990

AB Immunochem. and crystallog. studies were conducted on monoclonal antibody (D1.3) Fab-hen egg white lysozyme (HEL) complexes, unliganded D1.3 Fab, and

idiotype-antiidiotope interactions. The 3-dimensional structure of fab D1.3 showed that the relative disposition (quaternary structure) of the VH-VL and CH1-CL homol. subunits cannot be easily correlated with an antigen-bound or unbound state of the combining site. This angle was 138° in Fab D1.3 alone, 172° in the Fab D1.3-HEL complex, and 140° in its complex with Fab of a monoclonal antiidiotypic antibody (E225). This variability is consistent with the idea that the different elbow angles observed in Fab structures result from intrasegmental flexibility in antibody mols. Important conclusions concerning interaction between antigen and antibody in the Fab D1.3-HEL complex are as reported in A. Amit et al. (1986). In the Fab D1.3-Fab E225 complex, the 2 Fabs were roughly aligned along their major lengths. They differed in their elbow bending angles, which were 140° for D1.3 and 158° for E225. The complex was formed by interactions mostly between the hypervariable regions of the 2 Fabs. E225 carried an internal image of D1.3.

L16 ANSWER 30 OF 36 MEDLINE on STN
ACCESSION NUMBER: 1987241870 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2439094
TITLE: The structural basis of antigen-antibody recognition.
AUTHOR: Mariuzza R A; Phillips S E; Poljak R J
SOURCE: Annual review of biophysics and biophysical chemistry, (1987) Vol. 16, pp. 139-59. Ref: 62
Journal code: 8505748. ISSN: 0883-9182.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 7 Aug 1987
ED Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 7 Aug 1987
AB We have reviewed here the three-dimensional structure of an antigen-Fab complex as determined by X-ray crystallographic studies. The antigen is hen egg-white lysozyme (HEL), a protein whose three-dimensional structure and antigenic properties are well known. The Fab was prepared from a murine monoclonal anti-HEL antibody, IgG1,kappa, obtained by cell-hybridization techniques. The equilibrium association constant for the complex is 4.5 X 10(7) mol-1. The complex was crystallized and its three-dimensional structure was determined at 6-A and 2.8-A resolution. A three-dimensional model of the structure was built based on electron-density maps and the amino-acid sequence [determined from the nucleotide sequence of cDNA clones (M. Verhoeyen, C. Berek, J.M. Jarvis, G. Winter, in preparation)]. The three-dimensional structure of the complex shows that 17 antibody residues make close contacts (less than or equal to 4 A) with 16 antigen residues. Fifteen of the contacting antibody residues belong to the six complementarity-determining regions of the light chain (6 residues) and of the heavy chain (9 residues). The remaining two are located in regions of constant or nearly constant sequence ["framework" regions]. The 16 contacting lysozyme residues form a discontinuous, topographical determinant, since they are widely separated in the linear amino-acid sequence but are brought to relative spatial proximity by the three-dimensional folding of the polypeptide chain. The contacting surfaces are relatively flat, with protruding side chains of antigen and antibody penetrating each other over an area with maximum dimensions of 30 X 20 A. As in several other systems of protein-protein interactions, the

contacts are chemically characterized as van der Waals interactions and hydrogen bonds. Detailed analysis of the interactions reveals that the antibody's recognition of the antigen is finely specific and is affected by antigenic variation (as observed in lysozymes from other avian species). The quaternary structure of the complexed Fab is elongated, with the axes of the variable (VH + VL) and constant (CH1 + CL) domains making an angle close to 180 degrees. Comparison of the three-dimensional structure of the complexed lysozyme with that of native lysozyme showed no significant conformational change at the current resolution (2.8 A). Comparison of the Fab moiety of the complex with other Fabs of known three-dimensional structure suggested that upon complexing no conformational change takes place in the tertiary structure of Fab either.(ABSTRACT TRUNCATED AT 400 WORDS)

L16 ANSWER 31 OF 36 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 1987064655 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3097521
TITLE: Antibody Fab assembly: the interface residues between CH1 and CL.
AUTHOR: Padlan E A; Cohen G H; Davies D R
SOURCE: Molecular immunology, (1986 Sep) Vol. 23, No. 9, pp. 951-60. Journal code: 7905289. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198701
ENTRY DATE: Entered STN: 2 Mar 1990
Last Updated on STN: 2 Mar 1990
Entered Medline: 22 Jan 1987
ED Entered STN: 2 Mar 1990
Last Updated on STN: 2 Mar 1990
Entered Medline: 22 Jan 1987
AB The effective assembly of an antibody molecule requires the proper association of the light and heavy chains, namely the tight, canonical association of VH with VL, and of CH1 with CL. In this paper the interaction of CH1 is examined by looking at the degree of conservation of residues in the interface between CH1 and CL, where CH1 can belong to any of the heavy chain classes, and CL can be either lambda or kappa. The three-dimensional structures of four antibody Fabs have been examined to see which are the significant interacting residues and to see whether they also correspond to the conserved residues in the different classes. It was found that there are a few hydrophobic residues buried in the interface which make numerous contacts with residues of the other chain and which remain invariant, or else are highly conserved. Around the periphery of the interface there are numerous interacting residues that have appreciable variability. Within the interface there is a cavity, the function of which may be to permit some changes in the central interface residues while still preserving the same relative orientation of CH1 and CL.

L16 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:560818 CAPLUS Full-text
DOCUMENT NUMBER: 97:160818
ORIGINAL REFERENCE NO.: 97:26813a,26816a
TITLE: An unusual papain cleavage of a human IgG1 (λ) myeloma protein (Mot)
AUTHOR(S): Kojima, Mitsue; Odani, Shoji; Ono, Teruo
CORPORATE SOURCE: Prefect. Cancer Cent., Niigata Hosp., Niigata, 951, Japan
SOURCE: Molecular Immunology (1982), 19(9), 1095-103
CODEN: MOIMD5; ISSN: 0161-5890

DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB An IgG1 (λ) protein which showed a unique susceptibility towards papain digestion was isolated from the serum of a patient (Mot) with multiple myeloma. The Fab fragments of this protein were degraded rapidly into smaller peptides via an Fb fragment which corresponded to the constant domains (CL-CH1). Structural anal. of the isolated Fab fragment, which consisted of the intact heavy-chain, a 17,000 and a 5,000 mol. weight peptide fragment indicated that the initial cleavage site was located in the vicinity of the second hypervariable region of the Fd fragment. Examination of the partial amino acid sequences of the Mot heavy (H)-chain suggested that the variable region of the H-chain may be a hitherto unknown hybrid of subgroups I and III. This particular structure seems to have made the Fab fragment highly susceptible to papain. In the course of the present study, an intermediate 5 S fragment in the papain digests of several human IgG proteins was found which had previously been reported exclusively for the papain digest of rabbit IgG.

L16 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1982:560804 CAPLUS Full-text
DOCUMENT NUMBER: 97:160804
ORIGINAL REFERENCE NO.: 97:26809a,26812a
TITLE: The three-dimensional structure of a human IgG1 immunoglobulin at 4 .ANG. resolution: a computer fit of various structural domains on the electron density map
AUTHOR(S): Sarma, R.; Laudin, A. G.
CORPORATE SOURCE: Dep. Biochem., State Univ. New York, Stony Brook, NY, 11794, USA
SOURCE: Journal of Applied Crystallography (1982), 15(5), 476-81
CODEN: JACGAR; ISSN: 0021-8898
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB The crystal structure of an intact IgG1 mol. (DOB) was determined at a resolution of 4 Å from an electron d. map calculated with phases for the reflections derived by using the multiple isomorphous replacement method. The map was interpreted by rotation and translation of known structures of the various fragments of the IgG mol. The Fc fragment, the constant domains (CH1 and CL) of the Fab fragment, and the variable domains (VH and VL) of the Fab fragment were rotated and translated in the DOB unit cell and superimposed on the calculated electron d. map. The total number of rotational and translational parameters for each fragment was determined by using several known and expected features of the IgG mol. The superposition was quantitated by accumulating the electron d. values at the various α-carbon atoms. The 3 fragments investigated in each case gave 1 peak, thus unambiguously providing the parameters relating each fragment with the DOB mol. The final structure shows 2 possible ways of joining the CH1 domain of the Fab fragment with the CH2 domain of the Fc fragment. A refinement of the model is expected to resolve this ambiguity.

L16 ANSWER 34 OF 36 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 1981208100 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7236608
TITLE: Crystallographic refinement and atomic models of a human Fc fragment and its complex with fragment B of protein A from Staphylococcus aureus at 2.9- and 2.8-A resolution.
AUTHOR: Deisenhofer J
SOURCE: Biochemistry, (1981 Apr 28) Vol. 20, No. 9, pp. 2361-70.

Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198108
ENTRY DATE: Entered STN: 16 Mar 1990
Last Updated on STN: 16 Mar 1990
Entered Medline: 27 Aug 1981

ED Entered STN: 16 Mar 1990
Last Updated on STN: 16 Mar 1990
Entered Medline: 27 Aug 1981

AB The model of human Fc fragment was refined at 2.9-A resolution. Two different automated procedures for crystallographic refinement were used [Deisenhofer, J., & Steigemann, W. (1975) Acta Crystallogr., Sec. B B31, 238; Jack, A., & Levitt, M. (1978) Acta Crystallogr., Sect. A A34, 931]. The final R value is 0.22. The dimer of CH3 domains closely resembles the CH1-CL aggregate in Fab fragments. There is no contact between CH2 domains. The contact between CH2 and CH3 domains has about one-third of the size of the CH3-CH3 contact. The carbohydrate, a branched chain of nine hexose units, covers parts of the C-contact face of the CH2 domain, shielding hydrophobic residues on this surface. Six atoms of the carbohydrate are within hydrogen-bonding distance of atoms in the CH2 domain. Crystallographic refinement of the complex between Fc fragment and fragment B of protein A from Staphylococcus aureus reduced the R value of the model is 0.24. A major part of the structure of fragment B consists of two alpha helics; the rest of the polypeptide chain is folded irregularly. In the crystal, fragment B forms two contacts with Fc fragment molecules. Contact 1 involves residues from both helices of fragment B, and residues from the CH2 and CH3 domains of FC, and is predominantly hydrophobic. Contact 2 is smaller than contact 1. Residues from the second helix and adjacent residues of fragment B and residues only from the CH3 domain of Fc contribute to contact 2. The nature of contact 2 is mainly polar and includes a sulfate ion. There are strong arguments that contact 1 is the fragment B-Fc contact formed in solution under physiological conditions, while contact 2 is a crystal contact.

L16 ANSWER 35 OF 36 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 1976258962 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 955567
TITLE: Crystallographic structural studies of a human Fc-fragment. I. An electron-density map at 4 A resolution and a partial model.
AUTHOR: Deisenhofer J; Colman P M; Huber R; Haupt H; Schwick G
SOURCE: Hoppe-Seyler's Zeitschrift fur physiologische Chemie, (1976 Mar) Vol. 357, No. 3, pp. 435-45.
Journal code: 2985060R. ISSN: 0018-4888.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197611
ENTRY DATE: Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 1 Nov 1976

ED Entered STN: 13 Mar 1990
Last Updated on STN: 13 Mar 1990
Entered Medline: 1 Nov 1976

AB The crystal structure of a human Fc fragment was analysed at 4 A resolution. A partial interpretation of the electron-density map in terms of domain structure was possible. The molecule has the shape of a mickey mouse. The

spherical domain was interpreted visually and by domain Patterson function interpretation as the CH3 dimer. This dimer resembles closely the CH1-CL dimer found in Fab structures. The ellipsoidal "ears" of the molecule represent the CH2 domains. They are widely separated from each other, but closely connected to CH3. Their tertiary structure must be different from CH1, as Patterson domain interpretations were unsuccessful. A chain tracing in CH2 was not yet possible.

L16 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1973:451645 CAPLUS Full-text
DOCUMENT NUMBER: 79:51645
ORIGINAL REFERENCE NO.: 79:8341a,8344a
TITLE: Energy transfer distance measurements in immunoglobulins. II. Localization of the hapten binding sites and the interheavy chain disulfide bond in rabbit antibody
AUTHOR(S): Bunting, James R.; Cathou, Renata E.
CORPORATE SOURCE: Sch. Med., Tufts Univ., Boston, MA, USA
SOURCE: Journal of Molecular Biology (1973), 77(2), 223-35
CODEN: JMOBAK; ISSN: 0022-2836
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB The distance between the hapten combining site and the single interheavy chain SS bond in rabbit immunoglobulin G was determined by measuring the efficiency of energy transfer between chromophores specifically attached at these sites on the mol. The donor chromophore, Dns-lysine (Dns = dimethylaminonaphthalenesulfonyl-), was noncovalently bound in the combining sites of high-affinity antiDns antibody mols., in 1 case, and in the combining site of the pepsin Fab' fragment of antiDns in another. The acceptor chromophore, fluorescein, was covalently attached by SS interchange of bis(fluoresceinthiocarbamoyl)-DL-cystine with sulfhydryls generated by selective reduction of the interheavy chain SS bond of whole antiDns antibody and of the (Fab')2 pepsin fragment. The presence of acceptor decreased the donor fluorescence lifetime by .apprx.1.0 nsec in both cases, i.e., for the whole antibody, from 23.6 to 22.7 nsec, and for the Fab' fragment from 23.6 to 22.5 nsec. An average separation distance of 81 Å was calculated from an average observed transfer efficiency of 3.7%. This value agrees closely with the over-all length of a Fab' fragment of a human IgG myeloma protein. The antibody combining site is at, or very close to, the tip of the Fab fragment and the interheavy chain SS bond is at or near the edge of the CL-CH1 domain.

=> d his

(FILE 'HOME' ENTERED AT 07:25:29 ON 26 AUG 2008)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 07:25:43 ON 26 AUG 2008
E AXEN A/AU
L1 2 S E3
L2 45 S E5
E BAUMANN H/AU
L3 1328 S E3-E12
E E12
L4 101 S E4-E8
E BAUMANN HERB/AU
L5 73 S E4-E5
E CARREDANO E/AU

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L6            38 S E3-E4
L7          1559 S L1-L6
L8             1 S L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR
KAPPA-FAB)(5A)(CONSTANT))
L9             2 S L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR
KAPPA-FAB)(15A)(CONSTANT))
L10            2 DUP REM L9 (0 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 07:29:26 ON 26 AUG 2008
L11            0 S L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR
KAPPA-FAB)(5A)(CH1))

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 07:30:05 ON 26 AUG 2008
L12            5 S L7 AND ((IGG OR IMMUNOGLOBULIN OR ANTIBOD OR FAB OR K-FAB OR
KAPPA-FAB)(10A)(CH1))
L13            2 DUP REM L12 (3 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 07:31:01 ON 26 AUG 2008
L14            0 S (CH1-CL OR CL-CH1 OR (CH1(2A)CL) )(15A)(CONSTANT OR FAB)

     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 07:32:18 ON 26 AUG 2008
L15           70 S (CH1-CL OR CL-CH1 OR (CH1(2A)CL) )(15A)(CONSTANT OR FAB)
L16           36 DUP REM L15 (34 DUPLICATES REMOVED)

=> logoff hold
-12.80     -15.20

 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 07:32:47 ON 26 AUG 2008
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